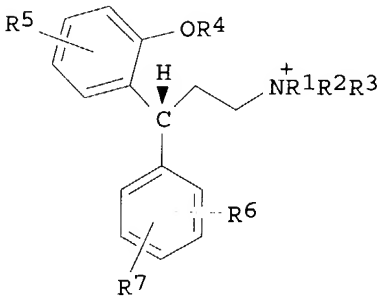
Inventors

L18 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:902176 HCAPLUS
DOCUMENT NUMBER: 141:379634
TITLE: A preparation of quaternary ammonium compounds, useful as antimuscarinic agents
INVENTOR(S): **Lennon, Patrick James; Bonafoux, Dominique Francoise; Wolfson, Sergey Gregory**
PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

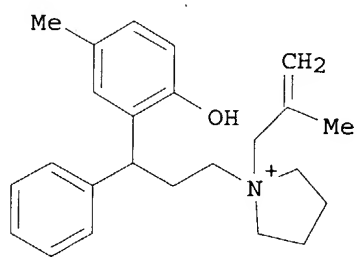
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004091607	A1	20041028	WO 2004-IB1290	20040413

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-462956P P 20030415
GI



I



II

AB The invention relates to a preparation of novel quaternary ammonium compds. of formula I•X- [wherein: R1, R2, and R3 are independently selected from (cyclo)alkyl, alk(en/yn)yl, cycloalkenyl, at least one of R1, R2, and R3 contains an unsatd. C-C bond, and any 2 of R1, R2, and R3 may form a ring with the quaternary ammonium nitrogen, etc.; R4 is H, Me, alkyl, or alkoxy, etc.; R5, R6, and R7 are independently selected from H, OMe, OH, C(O)NH2, halogen, or SO2NH2, etc.; X- is an anion of a pharmaceutically acceptable acid], useful as antimuscarinic agents (no biol. data). The prepared compds. are useful as medicaments for treatment of **asthma**, **chronic obstructive** pulmonary disease, allergic

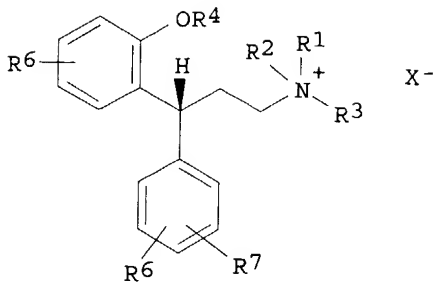
rhinitis, and **urinary** disorder, etc. (claimed). For instance, quaternary ammonium compound II•Br- was prepared via reductive amination of 6-methyl-4-phenyl-2-chromanol with pyrrolidine followed by quaternization with prop-2-enyl bromide (example 1, no yield data).

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:335062 HCAPLUS
DOCUMENT NUMBER: 138:353732
TITLE: Quaternary ammonium compounds and their use as antimuscarinic agents
INVENTOR(S): Richards, Ivan; Cammarata, Sue K.; Wegner, Craig D.; Hawley, Michael; Warchol, Mark P.; Kontny, Mark; Morozowich, Walter; Kolbasa, Karen P.; Moon, Malcolm W.; **Bonafoux, Dominique**; **Wolfson, Sergey G.**; **Lennon, Patrick J.**
PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003035599	A1	20030501	WO 2002-US34529		20021025
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2003158176	A1	20030821	US 2002-280906		20021025
BR 2002006207	A	20031223	BR 2002-6207		20021025
EP 1461306	A1	20040929	EP 2002-793840		20021025
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
NO 2003002938	A	20030825	NO 2003-2938		20030626
PRIORITY APPLN. INFO.:			US 2001-348930P	P	20011026
			US 2002-361979P	P	20020306
			US 2002-391521P	P	20020625
			WO 2002-US34529	W	20021025

OTHER SOURCE(S): MARPAT 138:353732
GI



I

AB Novel quaternary ammonium compds. I [R1-R3 = (un)substituted alkyl; NR1R2, NR2R3, NR1R3 = heterocyclic; R4 = H, Me,acyl, alkoxycarbonyl, (un)substituted NH2; R5-R7 = H, OMe, OH, CONH2, SO2NH2, F, Cl, Br, I, CF3, (un)substituted alkyl; X = anion of a pharmaceutically acceptable acid] were prepared for use as antimuscarinic agents. Thus, tolterodine tartrate was converted to the free base and quaternized with MeI to give (R)-5,2-Me(OH)C6H3CHPhCH2CH2N+(CHMe2)2Me I- which has high affinity, but little selectivity for M1-M5 muscarinic receptors.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:710769 HCAPLUS
DOCUMENT NUMBER: 137:241989
TITLE: IV magnesium sulfate in the treatment of acute severe **asthma**: a multicenter randomized controlled trial
AUTHOR(S): Silverman, Robert A.; Osborn, Harold; Runge, Jeffrey; Gallagher, E. John; Chiang, William; Feldman, James; Gaeta, Theodore; Freeman, Katherine; Levin, Bruce; Mancherje, Noel; Scharf, Steven; Kwiatkowski, Thomas; Arsove, Pamela; Bloch, Helen; Gabinskiy, Boris; Kirrane, Barbara; Paiano, Ruth; **Wolfson, Scott**; Green, Adam; Sprague, Mark; Ganz, Jason; Malin, Robert; Hanline, Philip; Spiegel, Bradley; Carter, Janet; Price, Marlow; Iacometta, David; Katzman, Daniel; Muratori, John; Fratello, Dominick; Blaufeux, Brian; Held, David; Kindshuh, Mark; Fuentes, Hector; Fish, Susan; Kayne, Herb; Melendez, Elliot; Luxenberg, Douglas; Tang, Mark; Shevlin, Lawrence; Schwartz, Robert; Rescorl, Ddonna; Chinchilla, Manuel; Bijur, Polly; Einstein, Albert; Abberton, James; Rosen, Abby
CORPORATE SOURCE: Acute Asthma/Magnesium Study Group, Department of Emergency Medicine, Long Island Jewish Medical Center, New Hyde Park, NY, USA
SOURCE: Chest (2002), 122(2), 489-497
CODEN: CHETBF; ISSN: 0012-3692
PUBLISHER: American College of Chest Physicians
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Studies of IV magnesium sulfate as a treatment for acute **asthma** have had mixed results, with some data suggesting a benefit for acute severe **asthma**, but not for mild-to-moderate **asthma**. In a multicenter cohort, this study tests the hypothesis that administration of magnesium sulfate improves pulmonary function in patients with acute severe **asthma**. Placebo-controlled,

double-blind, randomized clin. trial. Emergency departments (EDs) of eight hospitals. Patients aged 18 to 60 yr presenting with acute **asthma** and FEV1 ≤ 30% predicted on arrival to the ED. All patients received nebulized albuterol at regular intervals and IV methylprednisolone. Two grams of IV magnesium sulfate or placebo were administered 30 min after ED arrival. The primary efficacy end point was FEV1 at 240 min, and the data anal. was intent to treat. Two hundred forty-eight patients were included, and the mean FEV1 on ED arrival was 22.9% predicted. At 240 min, patients receiving magnesium had a mean FEV1 of 48.2% predicted, compared to 43.5% predicted in the placebo-treated group (mean difference, 4.7%; 95% confidence interval [CI], 0.29 to 9.3%; p = 0.045). A regression model confirmed the effect of magnesium compared to placebo was greater in patients with a lower initial FEV1 (p < 0.05). If the initial FEV1 was < 25% predicted, the final FEV1 was 45.3% predicted in the magnesium-treated group and 35.6% predicted in the placebo-treated group (mean difference, 9.7%; 95% CI, 4.0 to 15.3%; p = 0.001). If the initial FEV was ≥ 25% predicted, magnesium administration was not beneficial; the final FEV1 was 51.1% predicted in the magnesium-treated group and 53.9% predicted in the placebo-treated group (mean difference, - 2.9%, 95% CI, - 9.4 to 3.7; p = not significant). Overall, the use of magnesium sulfate did not improve hospital admission rates. Administration of 2 g of IV magnesium sulfate improves pulmonary function when used as an adjunct to standard therapy in patients with very severe, acute **asthma**.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:44580 HCAPLUS
DOCUMENT NUMBER: 120:44580
TITLE: Manganese complexes of nitrogen-containing macrocyclic ligands effective as catalysts for dismutating superoxide
INVENTOR(S): Aston, Karl William; **Lennon, Patrick James**; Modak, Anil Shrikrishna; Neuman, William Lojda; Riley, Dennis Patrick; Weiss, Randy Herman
PATENT ASSIGNEE(S): Monsanto Co., USA
SOURCE: Eur. Pat. Appl., 81 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 524161	A1	19930120	EP 1992-870097	19920702
R: PT				
CA 2072897	AA	19930120	CA 1992-2072897	19920702
CA 2072934	AA	19930120	CA 1992-2072934	19920702
WO 9302090	A1	19930204	WO 1992-US5805	19920702
W: AU, FI, JP, KR, NO				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
AU 9223383	A1	19930223	AU 1992-23383	19920702
AU 661023	B2	19950713		
EP 598753	A1	19940601	EP 1992-915849	19920702
EP 598753	B1	19980318		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
JP 06509566	T2	19941027	JP 1992-502872	19920702

AT 164164	E	19980415	AT 1992-915849		19920702
ES 2113952	T3	19980516	ES 1992-915849		19920702
JP 3155552	B2	20010409	JP 1993-502872		19920702
ZA 9205139	A	19930426	ZA 1992-5139		19920709
US 5610293	A	19970311	US 1995-442455		19950516
US 5637578	A	19970610	US 1995-442454		19950516
US 6084093	A	20000704	US 1995-442147		19950516
US 5874421	A	19990223	US 1995-469064		19950606
PRIORITY APPLN. INFO.:			US 1991-732853	A	19910719
			US 1992-829865	A	19920203
			US 1992-902146		19920626
			WO 1992-US5805	A	19920702
			US 1993-80732	A3	19930622

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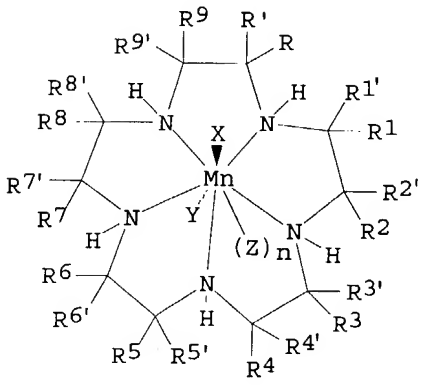


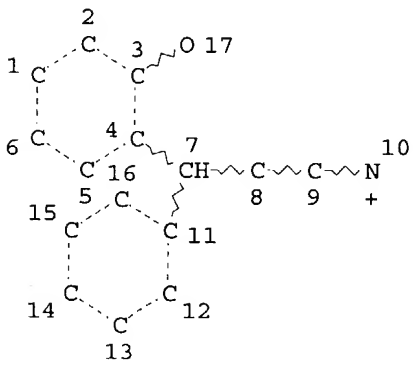
I

AB The present invention is directed to low-mol.-weight mimics of superoxide dismutase (SOD) represented by the formula I, wherein R,R',R1,R'1,R2,R'2,R3,R'3,R4,R'4,R5,R'5,R6,R'6,R7,R'7,R8,R'8,R9 and R'9 and X, Y, Z, and n are defined in the chains, useful as therapeutic agents for inflammatory disease states and disorders, ischemic/reperfusion injury, stroke, atherosclerosis, hypertension, and all other conditions of oxidant-induced tissue damage or injury.

FILE 'MEDLINE, EMBASE, BIOSIS, USPATFULL, USPAT2' ENTERED AT 11:31:45 ON 02 DEC 2004

L7 3 S L5
L8 3 DUP REM L7 (0 DUPLICATES REMOVED)
L9 3 S L8 AND (ASTH? OR COPD OR CHRONIC OBSTRU? OR ALERG? OR RHIN?

=> d que l9
L3 STR



NODE ATTRIBUTES:
CHARGE IS *+ AT 10
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE
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L9 3 SEA L8 AND (ASTH? OR COPD OR CHRONIC OBSTRU? OR ALERG? OR RHIN? OR COLD OR URIN?)

=> d l9 bib abs kwic 1-3

L9 ANSWER 1 OF 3 USPATFULL on STN
AN 2004:268373 USPATFULL
TI Combination therapies
IN Richards, Ivan Michael, Kalamazoo, MI, UNITED STATES
Manning, Robert Everett, St. Louis, MO, UNITED STATES
PA Pfizer Inc (U.S. corporation)
PI US 2004209916 A1 20041021
AI US 2004-824315 A1 20040413 (10)
PRAI US 2003-463975P 20030418 (60)
DT Utility
FS APPLICATION
LREP PFIZER INC., PATENT DEPARTMENT, MS8260-1611, EASTERN POINT ROAD, GROTON, CT, 06340
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN No Drawings

LN.CNT 1410
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention is directed to methods of treating **asthma**, **COPD**, allergic **rhinitis**, and infectious **rhinitis** by administering a first pharmaceutical agent including one or more compounds selected from the quarternary ammonium compounds of formulae I-V and a second pharmaceutical agent including one or more pharmaceutical agents selected from Adenosine A.sub.2a Receptor Agonists, D2-Dopamine Receptor Agonists, Phosphodiesterase Inhibitors (PDE's), corticosteroids, norepinephrine reuptake inhibitors, 4-hydroxy-7-[2-[2-[3-[2-phenylethoxy]-propylsulphonyl]ethylamino]ethyl]-1,3-benzothiazol-2(3H)-one, and pharmaceutically acceptable salts thereof, and non-quarternized antimuscarinic compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention is directed to methods of treating **asthma**, **COPD**, allergic **rhinitis**, and infectious **rhinitis** by administering a first pharmaceutical agent including one or more compounds selected from the quarternary ammonium compounds of formulae I-V. . .
SUMM [0002] The present invention concerns a method for the treatment of **asthma**, a group of breathing disorders termed **Chronic Obstructive** Pulmonary Disease (**COPD**), allergic **rhinitis**, and infectious **rhinitis**.
SUMM [0003] "**Asthma**" refers to a chronic lung disease causing bronchoconstriction (narrowing of the airways) due to inflammation (swelling) and tightening of the. . . the airways. The inflammation also causes an increase in mucus production, which causes coughing that may continue for extended periods. **Asthma** is generally characterized by recurrent episodes of breathlessness, wheezing, coughing, and chest tightness, termed exacerbations. The severity of exacerbations can. . . from mild to life threatening. The exacerbations can be a result of exposure to e.g. respiratory infections, dust, mold, pollen, **cold** air, exercise, stress, tobacco smoke, and air pollutants.
SUMM [0004] "**COPD**" refers to **Chronic Obstructive** Pulmonary Disease, primarily associated with past and present cigarette smoking. It involves airflow obstruction, mainly associated with emphysema and chronic. . .
SUMM [0005] "Allergic **rhinitis**" refers to acute **rhinitis** or nasal **rhinitis**, including hay fever. It is caused by allergens such as pollen or dust. It may produce sneezing, congestion, runny nose,. . .
SUMM [0006] "Infectious **rhinitis**" refers to acute **rhinitis** or nasal **rhinitis** of infectious origin. It is caused by upper respiratory tract infection by infectious **rhinoviruses**, coronaviruses, influenza viruses, parainfluenza viruses, respiratory syncytical virus, adenoviruses, coxsackieviruses, echoviruses, or Group A beta-hemolytic Streptococci and generically referred to as the common **cold**. It may produce sneezing, congestion, runny nose, and itchiness in the nose, throat, eyes, and ears.
SUMM [0007] In general, the invention features a method of treating **asthma**, **COPD**, allergic **rhinitis**, and infectious **rhinitis** by administering a first pharmaceutical agent including one or more compounds selected from the quarternary ammonium compounds of formulae I-V. . .
DETD [0042] In general, the invention features a method of treating **asthma**, **COPD**, allergic **rhinitis**, and infectious **rhinitis** by administering a first pharmaceutical

agent and a second pharmaceutical agent.

DETD [0101] The term "effective amount" refers to a therapeutically effective amount for treating **asthma**, **chronic obstructive** pulmonary disease (**COPD**), allergic **rhinitis**, or infectious **rhinitis**. The terms "therapy" and "therapeutically" encompass all kinds of treatments, including prophylaxis. In particular, "therapeutically effective" means that it is effective in preventing or arresting **COPD**. Also, it is to be understood that the initial dosage administered may be increased beyond the above upper level in. . .

DETD . . . for inhalation of various pharmaceutical agents are well known to those skilled in the art, including many aerosols for treating **asthma**. Aerosols may be produced with a nebulizer. Typically, the nebulizer is charged with a carrier solution and the compound in. . .

DETD . . . for inhalation of various pharmaceutical agents are well known to those skilled in the art, including many powders for treating **asthma**. When the dosage form is a powder, the compounds according to the invention can be administered in pure form or. . .

CLM What is claimed is:

1. A method of treating **chronic obstructive** pulmonary disease (**COPD**) in a mammal, comprising administering a first pharmaceutical agent and a second pharmaceutical agent, wherein the first pharmaceutical agent comprises. . .

2. A method of treating **chronic obstructive** pulmonary disease (**COPD**) in a mammal, which method comprises administering a first pharmaceutical agent and a second pharmaceutical agent, wherein the first pharmaceutical. . .

3. A method of treating **chronic obstructive** pulmonary disease (**COPD**) in a mammal, which method comprises administering a first pharmaceutical agent and a second pharmaceutical agent, wherein the first pharmaceutical. . .

4. A method of treating **chronic obstructive** pulmonary disease (**COPD**) in a mammal, which method comprises administering a first pharmaceutical agent and a second pharmaceutical agent, wherein the first pharmaceutical. . .

5. A method of treating **chronic obstructive** pulmonary disease (**COPD**) in a mammal, which method comprises administering a first pharmaceutical agent and a second pharmaceutical agent, wherein the first pharmaceutical. . .

13. A method of treating **chronic obstructive** pulmonary disease (**COPD**) in a mammal, comprising administering a first pharmaceutical agent and a second pharmaceutical agent, wherein the first pharmaceutical agent is. . .

IT 154189-40-9 **518360-66-2**, (3R)-3-(2-Hydroxy-5-methylphenyl)-N,N-diisopropyl-N-methyl-3-phenylpropan-1-aminium iodide **518360-67-3**, (3R)-3-(2-Hydroxy-5-methylphenyl)-N,N-diisopropyl-N-methyl-3-phenylpropan-1-aminium bromide **518360-68-4 518360-82-2 518360-83-3 518360-84-4 518360-85-5 518360-86-6 518360-87-7 518360-88-8 518360-89-9 518360-90-2 518360-91-3 518360-92-4 518360-93-5 686710-15-6**, (3R)-3-(2-Hydroxy-5-methylphenyl)-N,N-diisopropyl-N-methyl-3-phenylpropan-1-aminium 686745-68-6 688320-38-9 688364-67-2 688365-79-9 **777946-93-7 777946-94-8** 777946-95-9 777946-96-0 777946-97-1 777946-98-2 **777946-99-3 777947-00-9** 777947-01-0 **777947-02-1**
(combination therapies of asthma, COPD, allergic and infectious rhinitis)

L9 ANSWER 2 OF 3 USPATFULL on STN
AN 2003:226363 USPATFULL
TI Quaternary ammonium compounds
IN Richards, Ivan, Kalamazoo, MI, UNITED STATES
Cammarata, Sue K., Portage, MI, UNITED STATES
Wegner, Craig D., Mundelein, IL, UNITED STATES
Hawley, Michael, Kalamazoo, MI, UNITED STATES
Warchol, Mark Peter, Kalamazoo, MI, UNITED STATES
Kontny, Mark, Libertyville, IL, UNITED STATES
Morozowich, Walter, Kalamazoo, MI, UNITED STATES
Kolbasa, Karen Patrice, Schoolcraft, MI, UNITED STATES
Moon, Malcolm Wilson, Kalamazoo, MI, UNITED STATES
Bonafoux, Dominique, St. Louis, MO, UNITED STATES
Wolfson, Sergey Gregory, Chesterfield, MO, UNITED STATES
Lennon, Patrick James, Webster Groves, MO, UNITED STATES
PI US 2003158176 A1 20030821
AI US 2002-280906 A1 20021025 (10)
PRAI US 2001-348930P 20011026 (60)
US 2002-361979P 20020306 (60)
US 2002-391521P 20020625 (60)
DT Utility
FS APPLICATION
LREP DINSMORE & SHOHL, LLP, 1900 CHEMED CENTER, 255 EAST FIFTH STREET, CINCINNATI, OH, 45202
CLMN Number of Claims: 34
ECL Exemplary Claim: 1
DRWN 7 Drawing Page(s)
LN.CNT 1517
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel quaternary ammonium compounds of the formula ##STR1##

and any stereoisomers thereof, wherein R.sub.1, R.sub.2 and R.sub.3 independently represent C.sub.1-C.sub.6 alkyl, optionally substituted with phenyl or hydroxyl, or both, and wherein any two of R.sub.1, R.sub.2 and R.sub.3 may form a ring together with the quaternary ammonium nitrogen; R.sub.4 represents --H, --CH.sub.3, or --CO--R.sub.4-1,wherein R.sub.4-1 represents --(C.sub.1-C.sub.4 alkyl), --(C.sub.1-C.sub.4 alkoxy), or --NR.sub.4-2R.sub.4-3, wherein R.sub.4-2 and R.sub.4-3 independently represent --H or --(C.sub.1-C.sub.4 alkyl); R.sub.5, R.sub.6 and R.sub.7 independently represent --H, --OCH.sub.3, --OH, --CONH.sub.2, --SO.sub.2NH.sub.2, --F, --Cl, --Br, --I, --CF.sub.3, or --(C.sub.1-C.sub.4 alkyl), optionally substituted with one or two --OH, --(C.sub.1-C.sub.4 alkoxy), --COOH, or --CO--O--(C.sub.1-C.sub.3 alkyl); and X.sup.- represents an anion of a pharmaceutically acceptable acid, the compounds for use as medicaments, use of the compounds for the manufacture of specific medicaments, and pharmaceutical compositions comprising the compounds. The present invention also concerns a method of treatment involving administration of the compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM [0003] The novel compounds are useful as antimuscarinic agents. In particular, the novel compounds are useful for the treatment of **asthma**, a group of breathing disorders termed **Chronic Obstructive** Pulmonary Disease (**COPD**), allergic **rhinitis**, and **rhinorrhea** due to the common **cold**.
SUMM [0004] U.S. Pat. No. 5,382,600 discloses (substituted)

3,3-diphenylpropylamines useful for treating **urinary** incontinence. In particular, it discloses 2-[(1R)-3-(diisopropylamino)-1-phenylpropyl)-4-methylphenol, also known as N,N-diisopropyl-3-(2-hydroxy-5-methylphenyl)-3-phenylpropylamine, with the generic name of tolterodine, as being useful to treat **urinary** incontinence. Tolterodine is the compound of Example 22 of U.S. Pat. No. 5,382,600.

SUMM . . . tolterodine is a muscarinic receptor antagonist. It is presently being sold in a number of different countries for treatment of **urinary** incontinence under the name Detrol®, marketed by Pharmacia. When tolterodine is used to treat **urinary** incontinence it is administered perorally as a tablet. The major, active metabolite of tolterodine is the 5-hydroxymethyl derivative of tolterodine.

SUMM . . . Metabolism and Disposition, 26(4): 289-293 (1998) disclose hydroxytolterodine. U.S. Pat. No. 5,559,269 discloses this compound as being useful to treat **urinary** incontinence. Pharmacol. Toxicol., 81: 169-172 (1997) discloses that hydroxytolterodine has antimuscarinic activity.

SUMM . . . therapeutically active diarylpropylamines, which have favorable anticholinergic properties, and which can be used for the treatment of disorders related to **urinary** incontinence.

SUMM [0009] WO 02/34245 discloses the use of tolterodine for treating **asthma**, **COPD**, and allergic **rhinitis**.

SUMM . . . European Journal of Pharmacology (1999) 368:223-230, is concerned with the pharmacological effects of tolterodine, an antimuscarinic drug, in isolated human **urinary** bladder smooth muscle.

SUMM [0014] Stewart B H et al, The Journal of Urology (1976) 115:558-559 discloses therapy of mild to moderate stress **urinary** incontinence with a combination of phenylpropanolamine hydrochloride, chlorpheniramine maleate, and isopropamide iodide in a sustained release capsule.

SUMM . . . and other purposes, it is an object of the present invention to provide highly efficient pharmaceutical compounds for treatment of **asthma**.

SUMM [0018] It is also an object of the present invention to provide highly efficient pharmaceutical compounds for treatment of **Chronic Obstructive** Pulmonary Disease (**COPD**).

SUMM [0019] It is a further object of the present invention to provide highly efficient pharmaceutical compounds for treatment of allergic **rhinitis**.

SUMM [0020] It is an object of the present invention to provide highly efficient pharmaceutical compounds for treatment of **rhinorrhea** due to the common **cold**.

SUMM . . . invention provides use of a quaternary ammonium compound according to the invention for the manufacture of a medicament for treating **asthma**, **chronic obstructive** pulmonary disease (**COPD**), allergic **rhinitis**, **rhinorrhea** due to the common **cold**, or **urinary** disorder.

SUMM [0061] Finally, the present invention provides a method of treating **asthma**, **chronic obstructive** pulmonary disease (**COPD**), allergic **rhinitis**, **rhinorrhea** due to the common **cold**, or **urinary** disorder in a mammal, including man, comprising administering to said mammal, in need of such a treatment, a therapeutically effective. . .

DETD . . . have anti-cholinergic properties. Thus, they are useful for the treatment of acetylcholine-mediated disorders. In particular, they are useful for treating **asthma**, **chronic**

obstructive pulmonary disease (**COPD**), allergic **rhinitis**, and **rhinorrhea** due to the common **cold**.

DETD [0094] "**Asthma**" refers to a chronic lung disease causing bronchoconstriction (narrowing of the airways) due to inflammation (swelling) and tightening of the. . . the airways. The inflammation also causes an increase in mucus production, which causes coughing that may continue for extended periods. **Asthma** is characterized by recurrent episodes of breathlessness, wheezing, coughing, and chest tightness, termed exacerbations. The severity of exacerbations can range. . . from mild to life threatening. The exacerbations can be a result of exposure to e.g. respiratory infections, dust, mold, pollen, **cold** air, exercise, stress, tobacco smoke, and air pollutants.

DETD [0095] "**COPD**" refers to **Chronic Obstructive** Pulmonary Disease, primarily associated with past and present cigarette smoking. It involves airflow obstruction, mainly associated with emphysema and chronic. . .

DETD [0096] "Allergic **rhinitis**" refers to acute **rhinitis** or nasal **rhinitis**, including hay fever. It is caused by allergens such as pollen or dust. It may produce sneezing, congestion, runny nose,. . .

DETD [0097] "**Rhinorrhea** due to the common **cold**" refers to watery discharge from the nose in association with a virus infection, such as the common **cold**. The **rhinorrhea** may be caused by **rhinitis** due to a virus infection (such as the common **cold**).

DETD [0098] "**Urinary** disorders" and symptoms thereof include some or all of the following: urgency, frequency, incontinence, **urine** leakage, enuresis, dysuria, hesitancy, and difficulty of emptying bladder. In particular, **urinary** disorders include **urinary** incontinence, caused by e.g. unstable or overactive **urinary** bladder.

DETD [0099] Overactive **urinary** bladder encompasses variants of **urinary** disorders, including overactive detrusor (detrusor instability, detrusor hyperreflexia) and sensory urgency, as well as symptoms of detrusor overactivity, e.g. urge incontinence, urgency, **urinary** frequency, and LUTS (Lower **Urinary** Tract Symptoms), including obstructive **urinary** symptoms, such as slow **urination**, dribbling at the end of **urination**, inability to **urinate** and/or the need to strain to **urinate** at an acceptable rate, or irritating symptoms such as frequency, dry overactive bladder, and/or urgency).

DETD [0100] Other conditions are also included, which give rise to **urinary** frequency, urgency and/or urge incontinence. Overactive bladder disorders also include nocturia and mixed incontinence. While overactive bladder is often associated. . .

DETD [0104] The term "effective amount" refers to a therapeutically effective amount for treating **asthma**, **chronic obstructive** pulmonary disease (**COPD**), allergic **rhinitis**, **rhinorrhea** due to the common **cold**, or **urinary** disorder. The terms "therapy" and "therapeutically" encompass all kinds of treatments, including prophylaxis. In particular, "therapeutically effective" means that it. . .

DETD . . . for inhalation of various pharmaceutical agents are well known to those skilled in the art, including many aerosols for treating **asthma**.

DETD . . . for inhalation of various pharmaceutical agents are well known to those skilled in the art, including many powders for treating **asthma**. When the dosage form is a powder, the compounds

according to the invention can be administered in pure form or. . .

DETD [0113] For treatment of **rhinitis**, in particular **rhinitis** due to the common **cold**, the compounds according to the invention can advantageously be administered in combination with steroids, cromoglycates, and decongestants (alpha agonists). Such combination therapies are useful in the treatment of **rhinorrhea** due to the common **cold**.

DETD . . . spread systemically, the compounds according to the invention have an increased duration of action, with implications locally (i.e. for treating **asthma**, **chronic obstructive** pulmonary disease (**COPD**), allergic **rhinitis**, or **rhinorrhea** due to the common **cold**).

DETD [0257] A 65 year old female with a history of chronic **COPD** with FEV.sub.1 of 1.5 liters is treated with (3R)-3-(2-hydroxy-5-methylphenyl)-N,N-diisopropyl-N-methyl-3-phenylpropan-1-aminium iodide in an aerosol formulation, 1 mg every 12 hr continuously. . .

DETD [0258] A 50 year old male with a history of chronic **COPD** with FEV.sub.1/FVC of 60% is treated with (3R)-3-(2-hydroxy-5-methylphenyl)-N,N-diisopropyl-N-methyl-3-phenylpropan-1-aminium bromide in an aerosol formulation, 2 mg every 8 hr continuously for. . .

DETD [0259] A 25 year old female with a history of **asthma** with a morning peak flow of leas than 2 l/sec is treated with (3R)-3-(2-hydroxy-5-methylphenyl)-N,N-diisopropyl-N-methyl-3-phenylpropan-1-aminium iodide powder, 0.1 mg every 8. . .

DETD [0260] A 35 year old male with a history of severe **asthma** with a morning peak flow of 5 l/sec is treated with (3R)-3-(2-hydroxy-5-methylphenyl)-N,N-diisopropyl-N-methyl-3-phenylpropan-1-aminium bromide powder, 6 mg once a day continuously.. . .

DETD [0261] A 45 year old female with a history of severe **asthma** with a morning peak flow of less than 3 l/sec is treated with (3R)-3-(2-hydroxy-5-methylphenyl)-N,N-diisopropyl-N-methyl-3-phenylpropan-1-aminium iodide in an aerosol formulation, 2. . .

CLM What is claimed is:

. . . of a quaternary ammonium compound according to any one of claims 1-24 for the manufacture of a medicament for treating **asthma**.

. . . of a quaternary ammonium compound according to any one of claims 1-24 for the manufacture of a medicament for treating **chronic obstructive** pulmonary disease (**COPD**).

. . . of a quaternary ammonium compound according to any one of claims 1-24 for the manufacture of a medicament for treating **rhinorrhea** due to the common **cold**.

. . . a quaternary ammonium compound according to any one of claims 1-24 for the manufacture of a medicament for treating allergic **rhinitis**.

31. A method of treating **asthma** in a mammal, including man, comprising administering to said mammal, in need of such a treatment, a therapeutically effective amount. . .

32. A method of treating **chronic obstructive** pulmonary disease (**COPD**) in a mammal, including man, comprising administering to said mammal, in need of such a treatment, a therapeutically effective amount. . .

33. A method of treating allergic **rhinitis** in a mammal, including man, comprising administering to said mammal, in need of such a treatment, a therapeutically effective amount. . .

34. A method of treating **rhinorrhea** due to the common

cold in a mammal, including man, comprising administering to said mammal, in need of such a treatment, a therapeutically effective amount. . .

IT **518360-66-2P**
(prepn.of diarylpropylammonium salts as antimuscarinic agents)

IT **518360-67-3P 518360-68-4P** 518360-78-6P 518360-79-7P
518360-80-0P 518360-81-1P
(prepn.of diarylpropylammonium salts as antimuscarinic agents)

IT 518360-70-8P **518360-72-0P 518360-82-2P**
518360-83-3P 518360-84-4P 518360-85-5P
518360-86-6P 518360-87-7P 518360-88-8P
518360-89-9P 518360-90-2P 518360-91-3P
518360-92-4P 518360-93-5P 518360-94-6P
518360-95-7P 518360-96-8P 518360-97-9P
518360-98-0P 518360-99-1P 518361-00-7P
519038-88-1P
(prepn.of diarylpropylammonium salts as antimuscarinic agents)

L9 ANSWER 3 OF 3 USPATFULL on STN
AN 2002:301662 USPATFULL
TI Novel anticholinergic compounds and methods of use
IN Druzgala, Pascal, Santa Rosa, CA, UNITED STATES
PI US 2002169208 A1 20021114
AI US 2002-116202 A1 20020403 (10)
PRAI US 2001-281134P 20010403 (60)
US 2002-350516P 20020118 (60)
DT Utility
FS APPLICATION
LREP David R. Saliwanchik, Saliwanchik, Lloyd & Saliwanchik, A Professional Association, 2421 N.W. 41st Street, Suite A-1, Gainesville, FL, 32606-6669
CLMN Number of Claims: 48
ECL Exemplary Claim: 1
DRWN 7 Drawing Page(s)
LN.CNT 1041
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB In a preferred embodiment, the subject invention concerns novel analogs of oxybutynin. The present invention also concerns methods for synthesizing the oxybutynin analogs of the present invention. The invention also pertains to methods for treating patients suffering from incontinence and other conditions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . dry mouth, dysphagia, constipation, heartburn, change in taste perception, bloated feeling, paralytic ileus, dizziness, drowsiness, nervousness, disorientation, headache, weakness, insomnia, **urinary** retention or hesitancy, impotence, blurred vision, dilated pupils, photophobia, cycloplegia, precipitation acute glaucoma, flushing, decreased sweating, nasal congestion, and suppression. . .
SUMM [0009] **Asthma**, bronchitis and emphysema are known as **Chronic Obstructive** Pulmonary Diseases (**COPD**). **COPD** is characterized as generalized airways obstruction, particularly of small airways, associated with varying degrees of symptoms of chronic bronchitis, **asthma**, and emphysema. The term **COPD** was introduced because these conditions often coexist, and it may be difficult in an individual case to decide which is. . . intrinsic airways disease, from excessive collapse of airways during a forced expiration secondary to pulmonary emphysema, from bronchospasm as in **asthma**, or may be due to a combination of

these factors.

SUMM [0010] **Asthma** is characterized by increased responsiveness of the airway, resulting in airway obstruction. The underlying mechanisms causing **asthma** are unknown, but inherited or acquired imbalance of adrenergic and cholinergic control of airway diameter has been implicated. Overt **asthma** attacks may occur when individuals are subjected to various stresses, such as viral respiratory infection, exercise, emotional upset, nonspecific factors (e.g., changes in barometric pressure or temperature), inhalation of **cold** air or irritants (e.g., gasoline fumes, fresh paint and noxious odors, or cigarette smoke), exposure to specific allergens, and ingestion. . .

SUMM [0012] Many people are affected by **urinary** incontinence. Incontinence is particularly common in the elderly, **urinary** incontinence is present in approximately fifty percent of nursing home patients, and **urinary** incontinence is a well known urologic problem in women. It will affect nearly all women in some form during their. . .

SUMM [0013] Involuntary incontinence also known as urge incontinence and overactive bladder, occurs with a loss of a large volume of **urine** accompanied by symptoms of urgency, frequency and nocturia caused by an unstable bladder or detrusor instability. The patient may lose **urine** with a change in position or with auditory stimulation. The loss of small volumes of **urine** usually occurs because bladder over distension by a large amount of residual **urine** referred to as overflow incontinence.

SUMM . . . mixture of the R-enantiomer, R-oxybutynin, and the S-enantiomer, S-oxybutynin. Use of the S-enantiomer of oxybutynin, S-oxybutynin, for the treatment of **urinary** incontinence has been described in U.S. Pat. Nos. 5,532,278, and 5,736,577.

DETD . . . patients suffering from incontinence. Compounds of the subject invention can also be used for creating bronchodilation in patients suffering from **asthma** or obstructive airway disease. They can be used as mydriatic agents. In yet another embodiment, the compounds of the subject. . .

CLM What is claimed is:

45. The method, according to claim 44, used to treat **asthma** or obstructive airway disease.

IT

475090-48-3	475090-49-4	475090-50-7	475090-51-8	475090-52-9
475090-53-0	475090-54-1	475090-55-2	475090-56-3	
475090-57-4	475090-58-5	475090-59-6	475090-60-9	475090-61-0
475090-62-1	475090-63-2	475090-64-3	475090-65-4	475090-66-5
475090-67-6	475090-68-7	475090-69-8	475090-70-1	475090-71-2
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475091-07-7	475091-08-8	475091-09-9	475091-10-2	475091-11-3
475091-12-4	475091-13-5	**475091-14-6**	475091-15-7	
475091-16-8				

(novel anticholinergic compds. for treatment of incontinence and other disorders)

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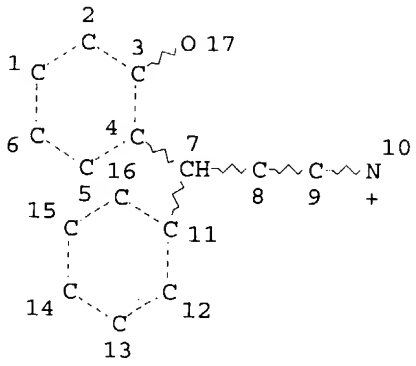
L3 STR



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DEFAULT ECLEVEL IS LIMITED

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NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE
L5 52 SEA FILE=REGISTRY SSS FUL L3
L6 5 SEA FILE=HCAPLUS ABB=ON PLU=ON L5
L10 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L6 AND (ASTH? OR COPD OR CHRONIC OBSTRU? OR ALERG? OR RHIN? OR COLD OR URIN?)
L11 5 SEA FILE=HCAPLUS ABB=ON PLU=ON L10 OR L6

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L11 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:902176 HCAPLUS
DOCUMENT NUMBER: 141:379634
TITLE: A preparation of quaternary ammonium compounds, useful as antimuscarinic agents
INVENTOR(S): Lennon, Patrick James; Bonafoux, Dominique Francoise; Wolfson, Sergey Gregory
PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004091607	A1	20041028	WO 2004-IB1290	20040413

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,

NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
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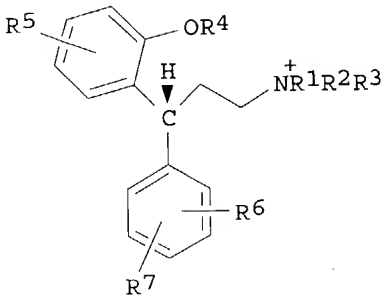
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
TD, TG

PRIORITY APPLN. INFO.: US 2003-462956P P 20030415

GI



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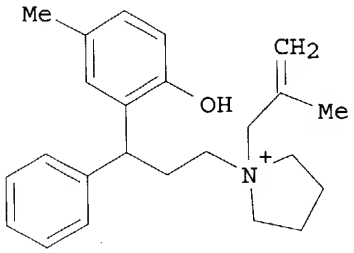


II

AB The invention relates to a preparation of novel quaternary ammonium compds. of formula I•X- [wherein: R1, R2, and R3 are independently selected from (cyclo)alkyl, alk(en/yn)yl, cycloalkenyl, at least one of R1, R2, and R3 contains an unsatd. C-C bond, and any 2 of R1, R2, and R3 may form a ring with the quaternary ammonium nitrogen, etc.; R4 is H, Me, alkyl, or alkoxy, etc.; R5, R6, and R7 are independently selected from H, OMe, OH, C(O)NH2, halogen, or SO2NH2, etc.; X- is an anion of a pharmaceutically acceptable acid], useful as antimuscarinic agents (no biol. data). The prepared compds. are useful as medicaments for treatment of **asthma**, **chronic obstructive** pulmonary disease, allergic **rhinitis**, and **urinary** disorder, etc. (claimed). For instance, quaternary ammonium compound II•Br- was prepared via reductive amination of 6-methyl-4-phenyl-2-chromanol with pyrrolidine followed by quaternization with prop-2-enyl bromide (example 1, no yield data).

IC ICM A61K031-40
ICS C07D295-096; A61P011-06; A61P011-02; A61P013-00; C07C215-66

CC 23-4 (Aliphatic Compounds)
Section cross-reference(s): 1, 27

IT Nose, disease
(allergic **rhinitis**, treatment of; preparation of quaternary ammonium compds., useful as antimuscarinic agents)

IT Lung, disease
(**chronic obstructive**, treatment of; preparation of quaternary ammonium compds., useful as antimuscarinic agents)

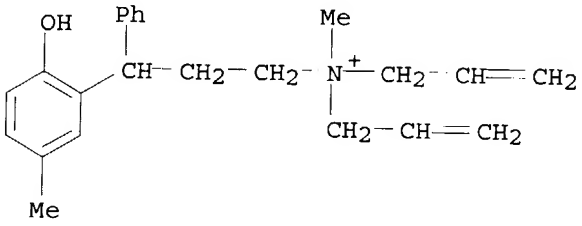
IT **Asthma**
Urinary tract, disease
(treatment of; preparation of quaternary ammonium compds., useful as antimuscarinic agents)

IT 777946-95-9P 777946-96-0P 777946-98-2P **777946-99-3P**
777947-00-9P 777947-01-0P **777947-02-1P**
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);

PREP (Preparation); USES (Uses)
(preparation of quaternary ammonium compds., useful as antimuscarinic agents)

IT **777946-99-3P 777947-00-9P 777947-02-1P**
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quaternary ammonium compds., useful as antimuscarinic agents)

RN 777946-99-3 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-N,5-dimethyl-γ-phenyl-N,N-di-2-propenyl-, iodide (9CI) (CA INDEX NAME)



● I⁻

RN 777947-00-9 HCAPLUS
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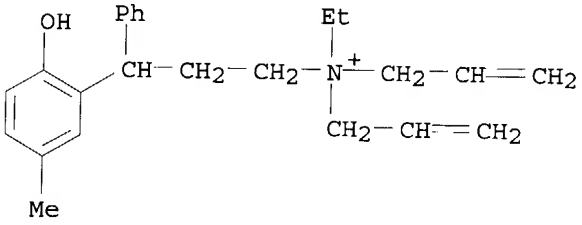
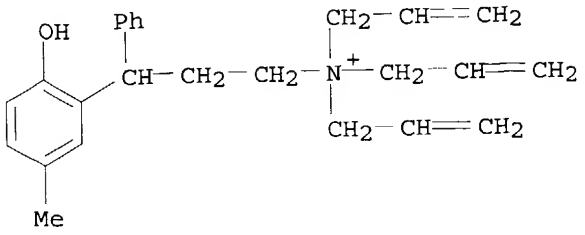


● I⁻

RN 777947-02-1 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-5-methyl-γ-phenyl-N,N,N-tri-2-propenyl-, bromide (9CI) (CA INDEX NAME)



● Br^-

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:902168 HCAPLUS
DOCUMENT NUMBER: 141:374727
TITLE: Method using quaternary ammonium compounds for the treatment of irritable bowel syndrome
INVENTOR(S): Richards, Ivan Michael; Kolbasa, Karen Patrice
PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004091597	A2	20041028	WO 2004-IB1218	20040405
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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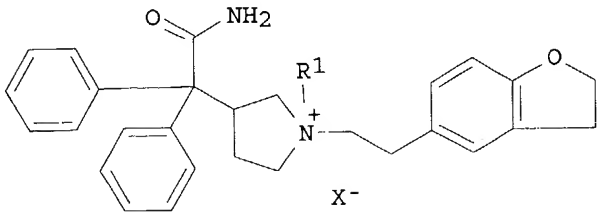
US 2004220224	A1	20041104	US 2004-823944	20040413
			US 2003-462921P P	20030415

PRIORITY APPLN. INFO.:
GI



I

AB The invention discloses a method for treating irritable bowel syndrome by administering quaternary ammonium compds. Compds. of the invention include e.g. I [R1 = (un)substituted C1-6 alkyl, (un)substituted CH2(C1-4 alkenyl), (un)substituted CH2(C1-6 alkynyl); X = anion of pharmaceutically acceptable acid]. Preparation of selected compds., e.g. (3R)-3-(2-hydroxy-5-methylphenyl)-N,N-diisopropyl-N-methyl-3-phenylpropan-1-aminium bromide, is included.

IC ICM A61K031-14
ICS A61P001-00; A61K031-4025

CC 1-9 (Pharmacology)
Section cross-reference(s): 25

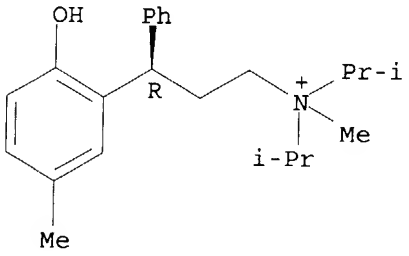
IT **518360-67-3P** 777946-95-9P 777946-96-0P 777946-98-2P
777946-99-3P 777947-00-9P 777947-01-0P
777947-02-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(quaternary ammonium compds. for treatment of irritable bowel syndrome)

IT **518360-66-2 518360-68-4 518360-82-2**
518360-83-3 518360-84-4 518360-85-5
518360-86-6 518360-87-7 518360-88-8
518360-89-9 518360-90-2 518360-91-3
518360-92-4 518360-93-5 518360-94-6
686710-15-6 688320-38-9 688364-67-2 688365-79-9
777946-93-7 782451-48-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quaternary ammonium compds. for treatment of irritable bowel syndrome)

IT **518360-67-3P 777946-99-3P 777947-00-9P**
777947-02-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(quaternary ammonium compds. for treatment of irritable bowel syndrome)

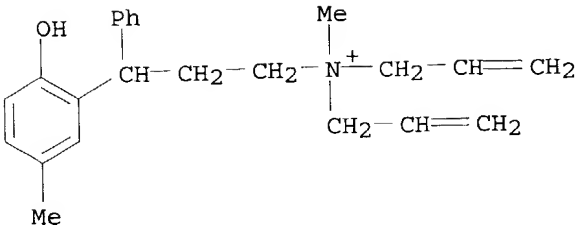
RN 518360-67-3 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-N,5-dimethyl-N,N-bis(1-methylethyl)-γ-phenyl-, bromide, (γR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



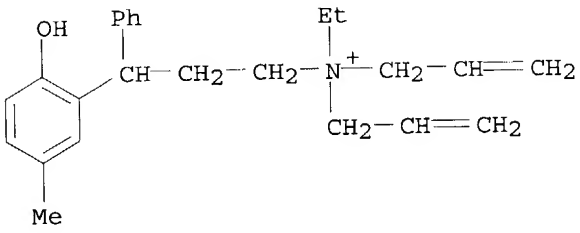
● Br^-

RN 777946-99-3 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-N,5-dimethyl-γ-phenyl-N,N-di-2-propenyl-, iodide (9CI) (CA INDEX NAME)



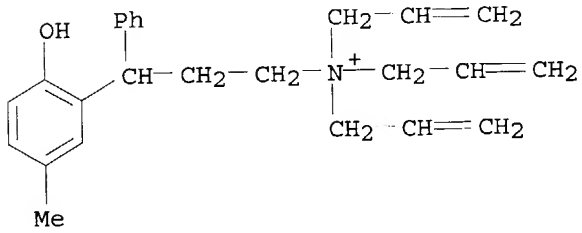
● I^-

RN 777947-00-9 HCAPLUS
CN Benzenepropanaminium, N-ethyl-2-hydroxy-5-methyl-γ-phenyl-N,N-di-2-propenyl-, iodide (9CI) (CA INDEX NAME)



● I^-

RN 777947-02-1 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-5-methyl-γ-phenyl-N,N,N-tri-2-propenyl-, bromide (9CI) (CA INDEX NAME)



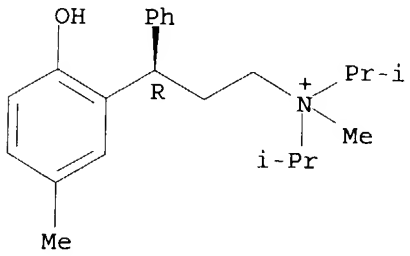
● Br^-

IT **518360-66-2 518360-68-4 518360-82-2**
518360-83-3 518360-84-4 518360-85-5
518360-86-6 518360-87-7 518360-88-8
518360-89-9 518360-90-2 518360-91-3
518360-92-4 518360-93-5 518360-94-6

686710-15-6 777946-93-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quaternary ammonium compds. for treatment of irritable bowel syndrome)

RN 518360-66-2 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-N,5-dimethyl-N,N-bis(1-methylethyl)-γ-phenyl-, iodide, (γR)- (9CI) (CA INDEX NAME)

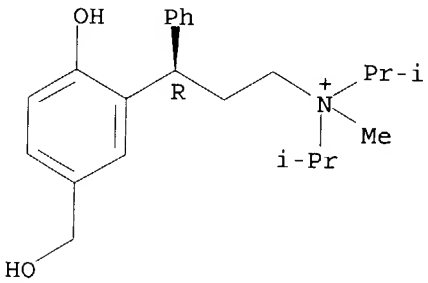
Absolute stereochemistry. Rotation (+).



● I^-

RN 518360-68-4 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-5-(hydroxymethyl)-N-methyl-N,N-bis(1-methylethyl)-γ-phenyl-, iodide, (γR)- (9CI) (CA INDEX NAME)

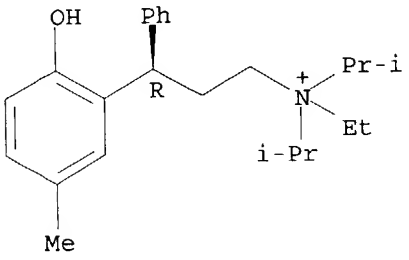
Absolute stereochemistry.



● I^-

RN 518360-82-2 HCAPLUS
CN Benzenepropanaminium, N-ethyl-2-hydroxy-5-methyl-N,N-bis(1-methylethyl)-γ-phenyl-, iodide, (γR)- (9CI) (CA INDEX NAME)

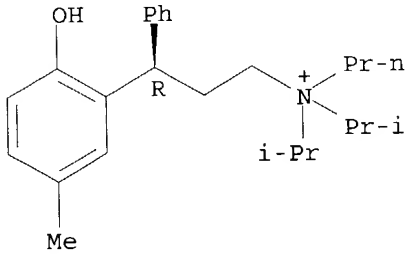
Absolute stereochemistry.



● I^-

RN 518360-83-3 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-5-methyl-N,N-bis(1-methylethyl)-γ-phenyl-N-propyl-, iodide, (γR)- (9CI) (CA INDEX NAME)

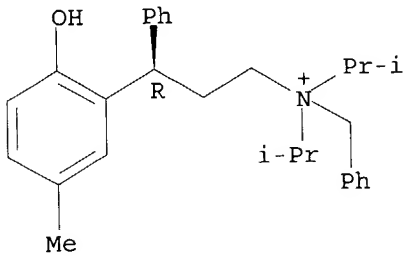
Absolute stereochemistry.



● I^-

RN 518360-84-4 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-5-methyl-N,N-bis(1-methylethyl)-γ-phenyl-N-(phenylmethyl)-, iodide, (γR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

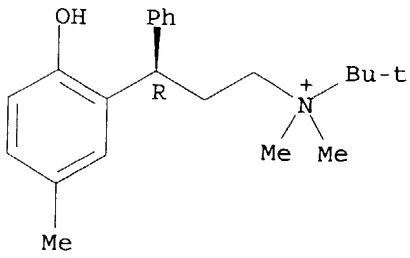


● I^-

RN 518360-85-5 HCAPLUS
CN Benzenepropanaminium, N-(1,1-dimethylethyl)-2-hydroxy-N,N,5-trimethyl-

γ-phenyl-, bromide, (γR)- (9CI) (CA INDEX NAME)

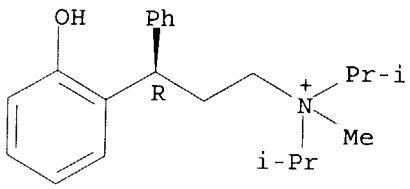
Absolute stereochemistry.



● Br^-

RN 518360-86-6 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-N-methyl-N,N-bis(1-methylethyl)-γ-phenyl-, bromide, (γR)- (9CI) (CA INDEX NAME)

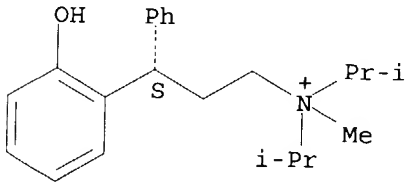
Absolute stereochemistry.



● Br^-

RN 518360-87-7 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-N-methyl-N,N-bis(1-methylethyl)-γ-phenyl-, bromide, (γS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

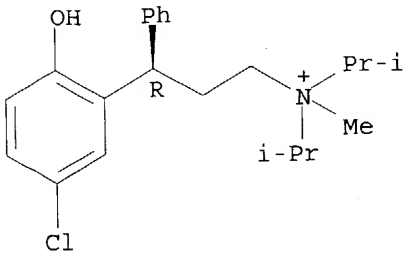


● Br^-

RN 518360-88-8 HCAPLUS
CN Benzenepropanaminium, 5-chloro-2-hydroxy-N-methyl-N,N-bis(1-methylethyl)-

γ-phenyl-, bromide, (γR)- (9CI) (CA INDEX NAME)

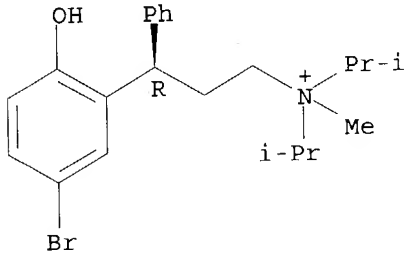
Absolute stereochemistry.



● Br^-

RN 518360-89-9 HCAPLUS
CN Benzenepropanaminium, 5-bromo-2-hydroxy-N-methyl-N,N-bis(1-methylethyl)-γ-phenyl-, bromide, (γR)- (9CI) (CA INDEX NAME)

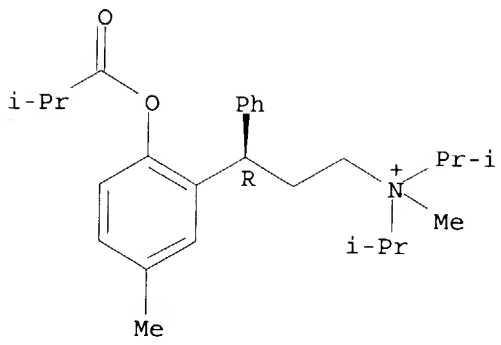
Absolute stereochemistry.



● Br^-

RN 518360-90-2 HCAPLUS
CN Benzenepropanaminium, N,5-dimethyl-N,N-bis(1-methylethyl)-2-(2-methyl-1-oxopropoxy)-γ-phenyl-, iodide, (γR)- (9CI) (CA INDEX NAME)

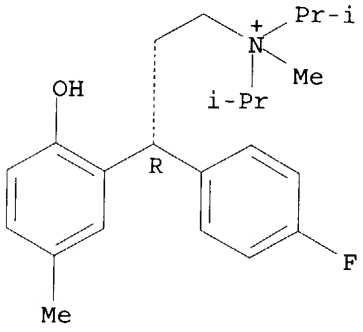
Absolute stereochemistry.



● I^-

RN 518360-91-3 HCAPLUS
CN Benzenepropanaminium, γ-(4-fluorophenyl)-2-hydroxy-N,5-dimethyl-N,N-bis(1-methylethyl)-, bromide, (γR)- (9CI) (CA INDEX NAME)

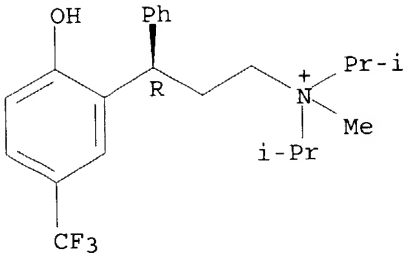
Absolute stereochemistry.



● Br^-

RN 518360-92-4 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-N-methyl-N,N-bis(1-methylethyl)-γ-phenyl-5-(trifluoromethyl)-, bromide, (γR)- (9CI) (CA INDEX NAME)

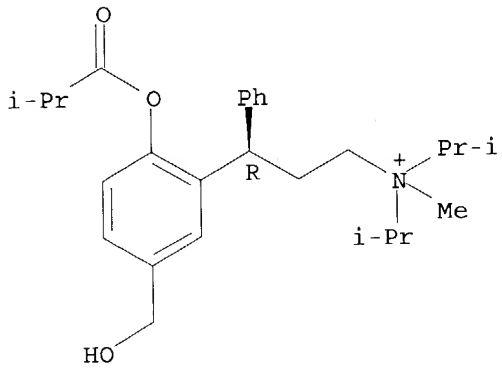
Absolute stereochemistry.



● Br^-

RN 518360-93-5 HCAPLUS
CN Benzenepropanaminium, 5-(hydroxymethyl)-N-methyl-N,N-bis(1-methylethyl)-2-(2-methyl-1-oxopropoxy)-γ-phenyl-, bromide, (γR)- (9CI) (CA INDEX NAME)

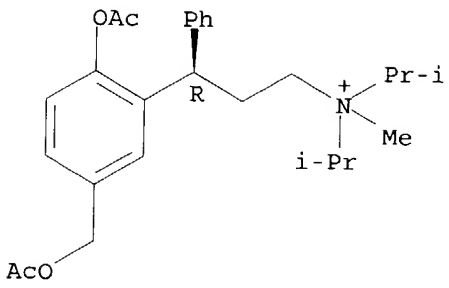
Absolute stereochemistry.



● Br^-

RN 518360-94-6 HCAPLUS
CN Benzenepropanaminium, 2-(acetyloxy)-5-[(acetyloxy)methyl]-N-methyl-N,N-bis(1-methylethyl)-γ-phenyl-, bromide, (γR)- (9CI) (CA INDEX NAME)

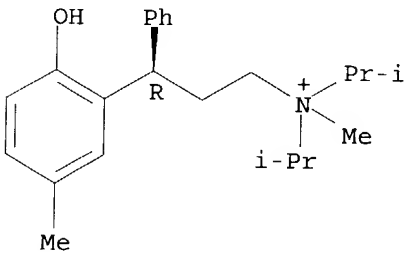
Absolute stereochemistry.



● Br^-

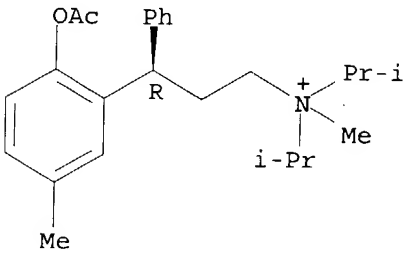
RN 686710-15-6 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-N,5-dimethyl-N,N-bis(1-methylethyl)-γ-phenyl-, (γR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 777946-93-7 HCAPLUS
CN Benzenepropanaminium, 2-(acetyloxy)-N,5-dimethyl-N,N-bis(1-methylethyl)-γ-phenyl-, iodide, (γR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● I^-

L11 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:878163 HCAPLUS
DOCUMENT NUMBER: 141:360690
TITLE: Combination therapies of **asthma**,

COPD, allergic and infectious **rhinitis**

INVENTOR(S): Richards, Ivan Michael; Manning, Robert Everett
PATENT ASSIGNEE(S): Pfizer Inc, USA
SOURCE: U.S. Pat. Appl. Publ., 20 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004209916	A1	20041021	US 2004-824315	20040413
WO 2004091596	A2	20041028	WO 2004-IB1170	20040405

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-463975P P 20030418

AB The invention is directed to methods of treating **asthma**, **COPD**, allergic **rhinitis**, and infectious **rhinitis** by administering a first pharmaceutical agent including one or more compds. selected from the quaternary ammonium compds. (Markush structures are included) and a second pharmaceutical agent including one or more pharmaceutical agents selected from Adenosine A 2a Receptor Agonists, D2-Dopamine Receptor Agonists, Phosphodiesterase Inhibitors (PDE's), corticosteroids, norepinephrine reuptake inhibitors, 4-hydroxy-7-[2-[2-[3-[2-phenylethoxy]-propylsulfonyl]ethylamino]ethyl]-1,3-benzothiazol-2(3H)-one, and pharmaceutically acceptable salts thereof, and non-quaternized antimuscarinic compds.

IC ICM A61K031-55
ICS A61K031-445; A61K031-40; A61K031-235; A61K031-195
NCL 514317000; 514408000; 514567000; 514532000; 514643000; 514554000
CC 1-9 (Pharmacology)
Section cross-reference(s): 2, 63
ST combination therapy **asthma COPD rhinitis** quaternary ammonium compds
IT Purinoceptor agonists
(A2, a; combination therapies of **asthma**, **COPD**, allergic and infectious **rhinitis**)
IT Adenosine receptors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A2A, agonists; combination therapies of **asthma**, **COPD**, allergic and infectious **rhinitis**)
IT Dopamine agonists
(D2; combination therapies of **asthma**, **COPD**, allergic and infectious **rhinitis**)
IT Nose, disease
(allergic **rhinitis**; combination therapies of **asthma**, **COPD**, allergic and infectious **rhinitis**)
IT Lung, disease

(**chronic obstructive**; combination therapies of **asthma**, **COPD**, allergic and infectious **rhinitis**)

IT **Asthma**
Combination chemotherapy
Drug delivery systems
Mammalia
Muscarinic antagonists
Stereoisomers
(combination therapies of **asthma**, **COPD**, allergic and infectious **rhinitis**)

IT Corticosteroids, biological studies
Quaternary ammonium compounds, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapies of **asthma**, **COPD**, allergic and infectious **rhinitis**)

IT Drug delivery systems
(inhalants; combination therapies of **asthma**, **COPD**, allergic and infectious **rhinitis**)

IT Nervous system agents
(noradrenaline reuptake inhibitors; combination therapies of **asthma**, **COPD**, allergic and infectious **rhinitis**)

IT Nose, disease
(**rhinitis**, infectious; combination therapies of **asthma**, **COPD**, allergic and infectious **rhinitis**)

IT 154189-40-9 **518360-66-2**, (3R)-3-(2-Hydroxy-5-methylphenyl)-N,N-diisopropyl-N-methyl-3-phenylpropan-1-aminium iodide **518360-67-3**, (3R)-3-(2-Hydroxy-5-methylphenyl)-N,N-diisopropyl-N-methyl-3-phenylpropan-1-aminium bromide **518360-68-4 518360-82-2**
518360-83-3 518360-84-4 518360-85-5
518360-86-6 518360-87-7 518360-88-8
518360-89-9 518360-90-2 518360-91-3
518360-92-4 518360-93-5 686710-15-6,
(3R)-3-(2-Hydroxy-5-methylphenyl)-N,N-diisopropyl-N-methyl-3-phenylpropan-1-aminium 686745-68-6 688320-38-9 688364-67-2 688365-79-9
777946-93-7 777946-94-8 777946-95-9 777946-96-0
777946-97-1 777946-98-2 **777946-99-3 777947-00-9**
777947-01-0 **777947-02-1**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapies of **asthma**, **COPD**, allergic and infectious **rhinitis**)

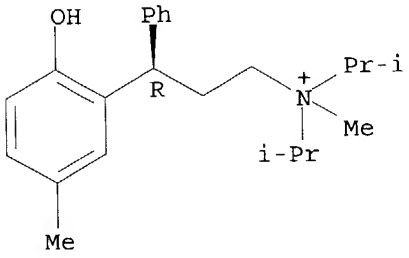
IT 9025-82-5, Phosphodiesterase
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors; combination therapies of **asthma**, **COPD**, allergic and infectious **rhinitis**)

IT **518360-66-2**, (3R)-3-(2-Hydroxy-5-methylphenyl)-N,N-diisopropyl-N-methyl-3-phenylpropan-1-aminium iodide **518360-67-3**, (3R)-3-(2-Hydroxy-5-methylphenyl)-N,N-diisopropyl-N-methyl-3-phenylpropan-1-aminium bromide **518360-68-4 518360-82-2**
518360-83-3 518360-84-4 518360-85-5
518360-86-6 518360-87-7 518360-88-8
518360-89-9 518360-90-2 518360-91-3
518360-92-4 518360-93-5 686710-15-6,
(3R)-3-(2-Hydroxy-5-methylphenyl)-N,N-diisopropyl-N-methyl-3-phenylpropan-

1-aminium **777946-93-7 777946-94-8 777946-99-3 777947-00-9 777947-02-1**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapies of **asthma**, **COPD**, allergic and infectious **rhinitis**)

RN 518360-66-2 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-N,5-dimethyl-N,N-bis(1-methylethyl)-γ-phenyl-, iodide, (γR)- (9CI) (CA INDEX NAME)

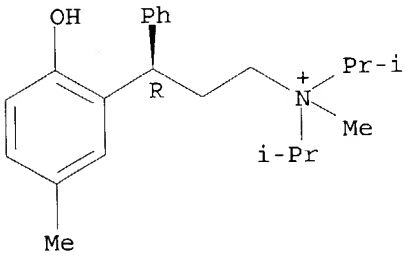
Absolute stereochemistry. Rotation (+).



● I^-

RN 518360-67-3 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-N,5-dimethyl-N,N-bis(1-methylethyl)-γ-phenyl-, bromide, (γR)- (9CI) (CA INDEX NAME)

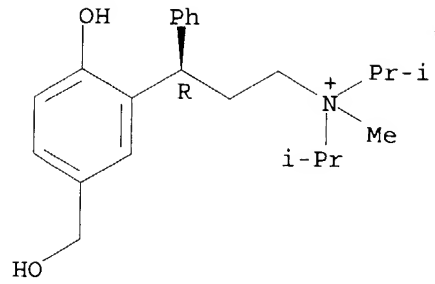
Absolute stereochemistry. Rotation (+).



● Br^-

RN 518360-68-4 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-5-(hydroxymethyl)-N-methyl-N,N-bis(1-methylethyl)-γ-phenyl-, iodide, (γR)- (9CI) (CA INDEX NAME)

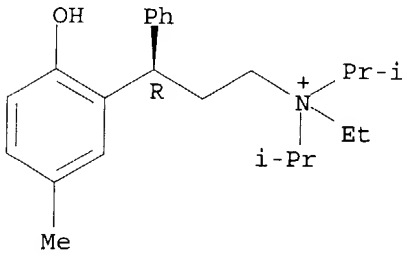
Absolute stereochemistry.



● I^-

RN 518360-82-2 HCAPLUS
CN Benzenepropanaminium, N-ethyl-2-hydroxy-5-methyl-N,N-bis(1-methylethyl)-γ-phenyl-, iodide, (γR)- (9CI) (CA INDEX NAME)

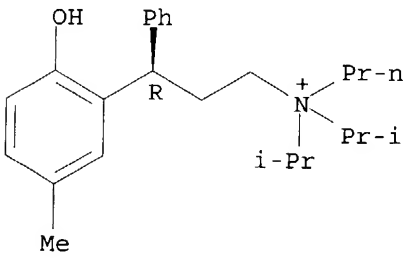
Absolute stereochemistry.



● I^-

RN 518360-83-3 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-5-methyl-N,N-bis(1-methylethyl)-γ-phenyl-N-propyl-, iodide, (γR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

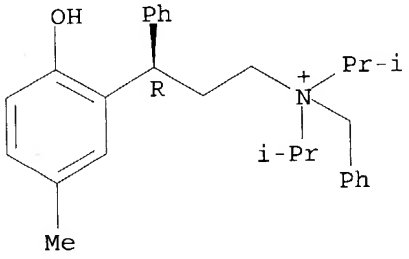


● I^-

RN 518360-84-4 HCAPLUS

CN Benzenepropanaminium, 2-hydroxy-5-methyl-N,N-bis(1-methylethyl)-γ-phenyl-N-(phenylmethyl)-, iodide, (γR)- (9CI) (CA INDEX NAME)

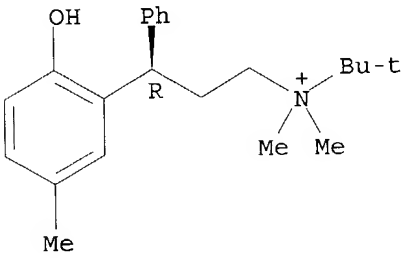
Absolute stereochemistry.



● I^-

RN 518360-85-5 HCAPLUS
CN Benzenepropanaminium, N-(1,1-dimethylethyl)-2-hydroxy-N,N,5-trimethyl-γ-phenyl-, bromide, (γR)- (9CI) (CA INDEX NAME)

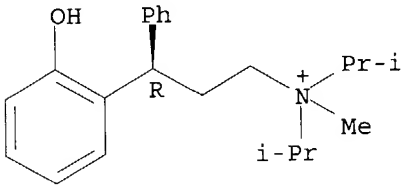
Absolute stereochemistry.



● Br^-

RN 518360-86-6 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-N-methyl-N,N-bis(1-methylethyl)-γ-phenyl-, bromide, (γR)- (9CI) (CA INDEX NAME)

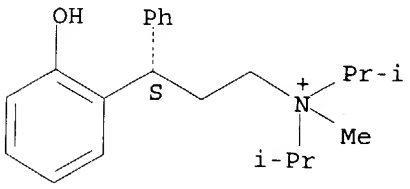
Absolute stereochemistry.



● Br^-

RN 518360-87-7 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-N-methyl-N,N-bis(1-methylethyl)-γ-phenyl-, bromide, (γS)- (9CI) (CA INDEX NAME)

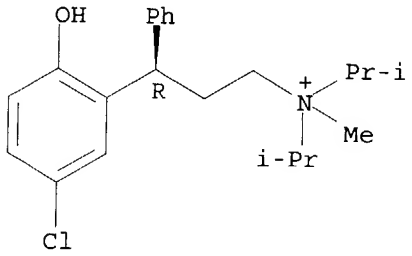
Absolute stereochemistry.



● Br^-

RN 518360-88-8 HCAPLUS
CN Benzenepropanaminium, 5-chloro-2-hydroxy-N-methyl-N,N-bis(1-methylethyl)-γ-phenyl-, bromide, (γR)- (9CI) (CA INDEX NAME)

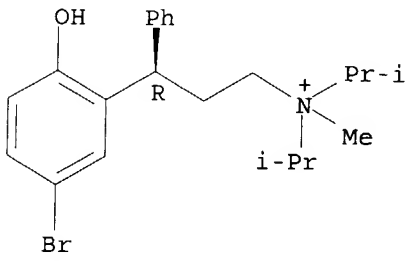
Absolute stereochemistry.



● Br^-

RN 518360-89-9 HCAPLUS
CN Benzenepropanaminium, 5-bromo-2-hydroxy-N-methyl-N,N-bis(1-methylethyl)-γ-phenyl-, bromide, (γR)- (9CI) (CA INDEX NAME)

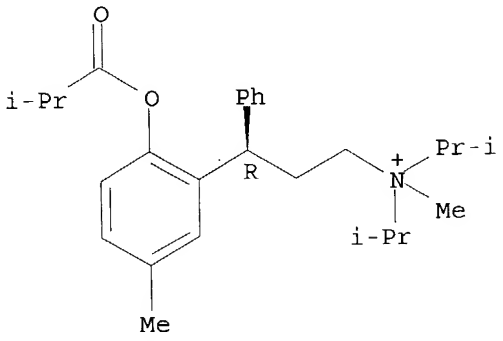
Absolute stereochemistry.



● Br^-

RN 518360-90-2 HCAPLUS
CN Benzenepropanaminium, N,5-dimethyl-N,N-bis(1-methylethyl)-2-(2-methyl-1-oxopropoxy)-γ-phenyl-, iodide, (γR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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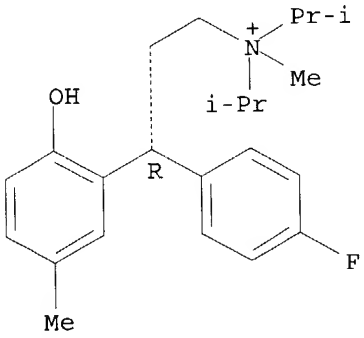
RN 518360-91-3 HCAPLUS
CN Benzenepropanaminium, γ-(4-fluorophenyl)-2-hydroxy-N,5-dimethyl-N,N-bis(1-methylethyl)-, bromide, (γR)- (9CI) (CA INDEX NAME)

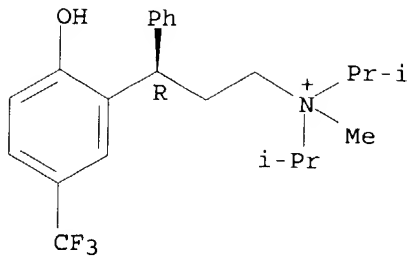
Absolute stereochemistry.



● Br^-

RN 518360-92-4 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-N-methyl-N,N-bis(1-methylethyl)-γ-phenyl-5-(trifluoromethyl)-, bromide, (γR)- (9CI) (CA INDEX NAME)

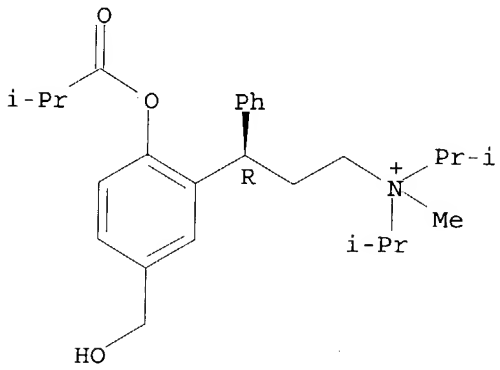
Absolute stereochemistry.



● Br^-

RN 518360-93-5 HCAPLUS
CN Benzenepropanaminium, 5-(hydroxymethyl)-N-methyl-N,N-bis(1-methylethyl)-2-(2-methyl-1-oxopropoxy)-γ-phenyl-, bromide, (γR)- (9CI) (CA INDEX NAME)

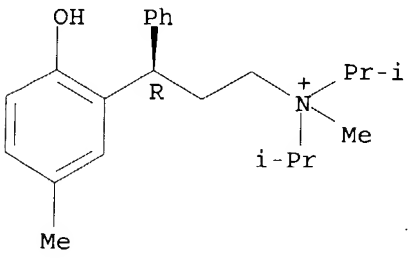
Absolute stereochemistry.



● Br^-

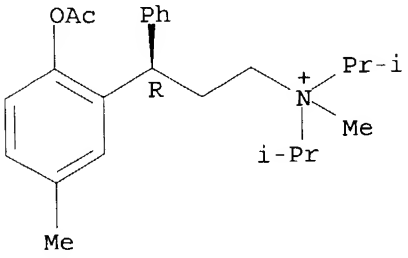
RN 686710-15-6 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-N,5-dimethyl-N,N-bis(1-methylethyl)-γ-phenyl-, (γR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 777946-93-7 HCAPLUS
CN Benzenepropanaminium, 2-(acetyloxy)-N,5-dimethyl-N,N-bis(1-methylethyl)-γ-phenyl-, iodide, (γR)- (9CI) (CA INDEX NAME)

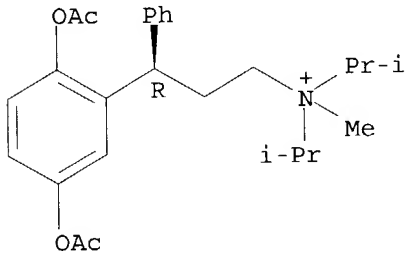
Absolute stereochemistry.



● I^-

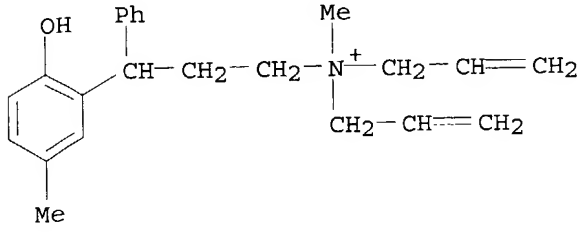
RN 777946-94-8 HCAPLUS
CN Benzenepropanaminium, 2,5-bis(acetyloxy)-N-methyl-N,N-bis(1-methylethyl)-γ-phenyl-, bromide, (γR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



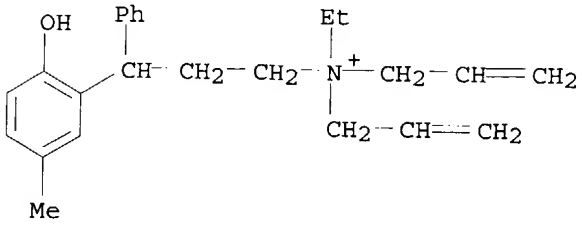
● Br^-

RN 777946-99-3 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-N,5-dimethyl-γ-phenyl-N,N-di-2-propenyl-, iodide (9CI) (CA INDEX NAME)



● I^-

RN 777947-00-9 HCAPLUS
CN Benzenepropanaminium, N-ethyl-2-hydroxy-5-methyl-γ-phenyl-N,N-di-2-propenyl-, iodide (9CI) (CA INDEX NAME)



● I^-

RN 777947-02-1 HCAPLUS
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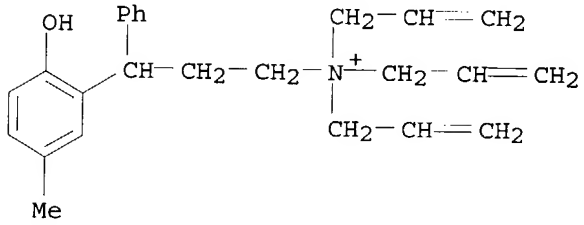


● Br^-

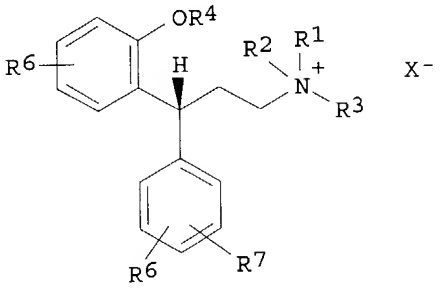
L11 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:335062 HCAPLUS
DOCUMENT NUMBER: 138:353732
TITLE: Quaternary ammonium compounds and their use as antimuscarinic agents
INVENTOR(S): Richards, Ivan; Cammarata, Sue K.; Wegner, Craig D.; Hawley, Michael; Warchol, Mark P.; Kontny, Mark; Morozowich, Walter; Kolbasa, Karen P.; Moon, Malcolm W.; Bonafoux, Dominique; Wolfson, Sergey G.; Lennon, Patrick J.
PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2003035599	A1	20030501	WO 2002-US34529 20021025
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW		
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG		
US 2003158176	A1	20030821	US 2002-280906 20021025
BR 2002006207	A	20031223	BR 2002-6207 20021025
EP 1461306	A1	20040929	EP 2002-793840 20021025
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK		
NO 2003002938	A	20030825	NO 2003-2938 20030626
PRIORITY APPLN. INFO.:			US 2001-348930P P 20011026
			US 2002-361979P P 20020306
			US 2002-391521P P 20020625
			WO 2002-US34529 W 20021025

OTHER SOURCE(S): MARPAT 138:353732

GI



I

AB Novel quaternary ammonium compds. I [R1-R3 = (un)substituted alkyl; NR1R2, NR2R3, NR1R3 = heterocyclic; R4 = H, Me,acyl, alkoxycarbonyl, (un)substituted NH2; R5-R7 = H, OMe, OH, CONH2, SO2NH2, F, Cl, Br, I, CF3, (un)substituted alkyl; X = anion of a pharmaceutically acceptable acid] were prepared for use as antimuscarinic agents. Thus, tolterodine tartrate was converted to the free base and quaternized with MeI to give (R)-5,2-Me(OH)C6H3CHPhCH2CH2N+(CHMe2)2Me I- which has high affinity, but little selectivity for M1-M5 muscarinic receptors.

IC ICM C07C211-27
ICS C07C211-29; C07C215-54; C07C215-66; C07C219-28; C07D295-02; C07C217-62; A61K031-14; A61K031-452; A61K031-40; A61P011-00

CC 25-4 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1

IT Nose, disease
(allergic **rhinitis**; prepn.of diarylpropylammonium salts as antimuscarinic agents)

IT Lung, disease
(**chronic obstructive**; prepn.of diarylpropylammonium salts as antimuscarinic agents)

IT Antiasthmatics
Asthma

Muscarinic antagonists
(prepn.of diarylpropylammonium salts as antimuscarinic agents)

IT **518360-66-2P**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn.of diarylpropylammonium salts as antimuscarinic agents)

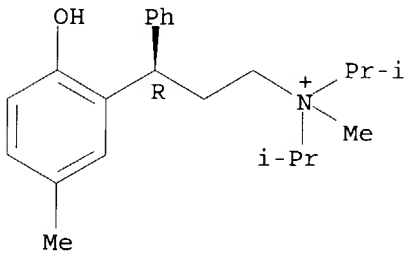
IT **518360-67-3P 518360-68-4P** 518360-78-6P 518360-79-7P
518360-80-0P 518360-81-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn.of diarylpropylammonium salts as antimuscarinic agents)

IT 518360-70-8P **518360-72-0P 518360-82-2P**
518360-83-3P 518360-84-4P 518360-85-5P
518360-86-6P 518360-87-7P 518360-88-8P
518360-89-9P 518360-90-2P 518360-91-3P
518360-92-4P 518360-93-5P 518360-94-6P
518360-95-7P 518360-96-8P 518360-97-9P
518360-98-0P 518360-99-1P 518361-00-7P
519038-88-1P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn.of diarylpropylammonium salts as antimuscarinic agents)

IT **518360-66-2P**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn.of diarylpropylammonium salts as antimuscarinic agents)

RN 518360-66-2 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-N,5-dimethyl-N,N-bis(1-methylethyl)-γ-phenyl-, iodide, (γR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

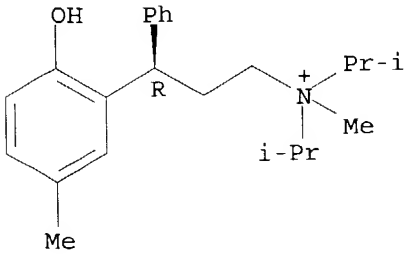


● I^-

IT **518360-67-3P 518360-68-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn.of diarylpropylammonium salts as antimuscarinic agents)

RN 518360-67-3 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-N,5-dimethyl-N,N-bis(1-methylethyl)-γ-phenyl-, bromide, (γR)- (9CI) (CA INDEX NAME)

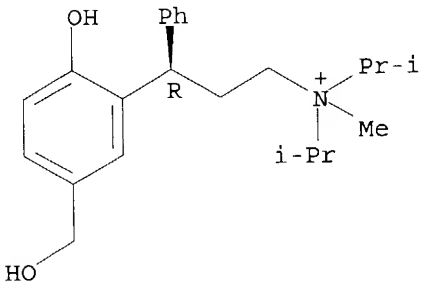
Absolute stereochemistry. Rotation (+).



● Br^-

RN 518360-68-4 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-5-(hydroxymethyl)-N-methyl-N,N-bis(1-methylethyl)-γ-phenyl-, iodide, (γR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

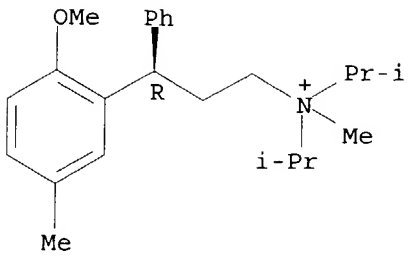


● I^-

IT **518360-72-0P 518360-82-2P 518360-83-3P**
518360-84-4P 518360-85-5P 518360-86-6P
518360-87-7P 518360-88-8P 518360-89-9P
518360-90-2P 518360-91-3P 518360-92-4P
518360-93-5P 518360-94-6P 518360-95-7P
518360-96-8P 518360-97-9P 518360-98-0P
518360-99-1P 518361-00-7P 519038-88-1P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn.of diarylpropylammonium salts as antimuscarinic agents)

RN 518360-72-0 HCAPLUS
CN Benzenepropanaminium, 2-methoxy-N,5-dimethyl-N,N-bis(1-methylethyl)-γ-phenyl-, iodide, (γR)- (9CI) (CA INDEX NAME)

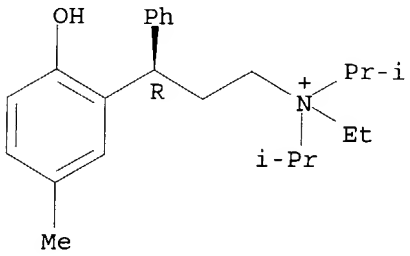
Absolute stereochemistry. Rotation (+).



● I^-

RN 518360-82-2 HCAPLUS
CN Benzenepropanaminium, N-ethyl-2-hydroxy-5-methyl-N,N-bis(1-methylethyl)-γ-phenyl-, iodide, (γR)- (9CI) (CA INDEX NAME)

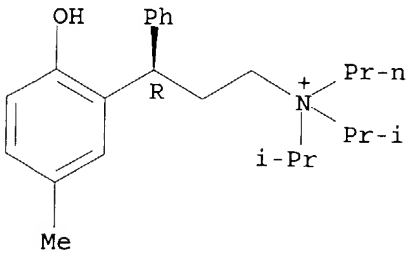
Absolute stereochemistry.



● I^-

RN 518360-83-3 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-5-methyl-N,N-bis(1-methylethyl)-γ-phenyl-N-propyl-, iodide, (γR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

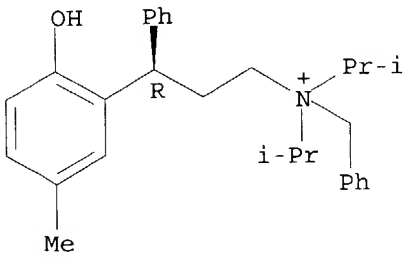


● I^-

RN 518360-84-4 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-5-methyl-N,N-bis(1-methylethyl)-γ-

phenyl-N-(phenylmethyl)-, iodide, (γR)- (9CI) (CA INDEX NAME)

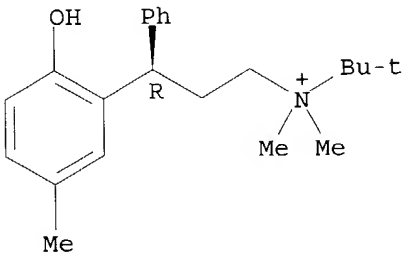
Absolute stereochemistry.



● I^-

RN 518360-85-5 HCAPLUS
CN Benzenepropanaminium, N-(1,1-dimethylethyl)-2-hydroxy-N,N,5-trimethyl-γ-phenyl-, bromide, (γR)- (9CI) (CA INDEX NAME)

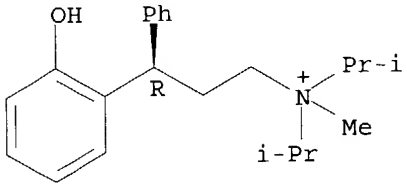
Absolute stereochemistry.



● Br^-

RN 518360-86-6 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-N-methyl-N,N-bis(1-methylethyl)-γ-phenyl-, bromide, (γR)- (9CI) (CA INDEX NAME)

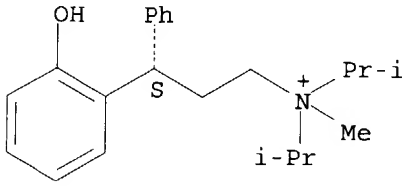
Absolute stereochemistry.



● Br^-

RN 518360-87-7 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-N-methyl-N,N-bis(1-methylethyl)-γ-phenyl-, bromide, (γS)- (9CI) (CA INDEX NAME)

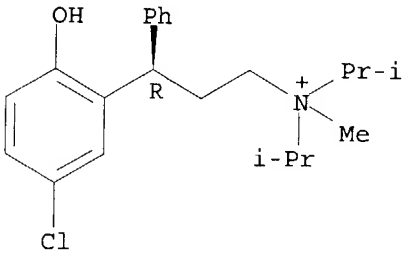
Absolute stereochemistry.



● Br^-

RN 518360-88-8 HCAPLUS
CN Benzenepropanaminium, 5-chloro-2-hydroxy-N-methyl-N,N-bis(1-methylethyl)-γ-phenyl-, bromide, (γR)- (9CI) (CA INDEX NAME)

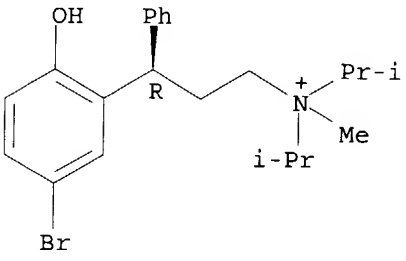
Absolute stereochemistry.



● Br^-

RN 518360-89-9 HCAPLUS
CN Benzenepropanaminium, 5-bromo-2-hydroxy-N-methyl-N,N-bis(1-methylethyl)-γ-phenyl-, bromide, (γR)- (9CI) (CA INDEX NAME)

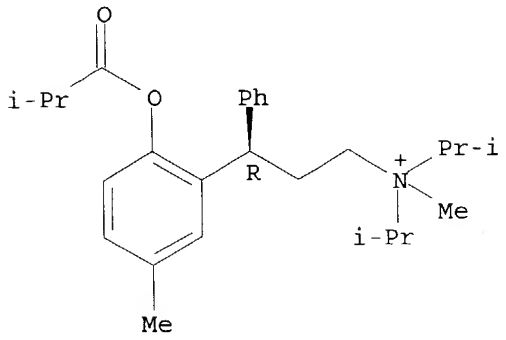
Absolute stereochemistry.



● Br^-

RN 518360-90-2 HCAPLUS
CN Benzenepropanaminium, N,5-dimethyl-N,N-bis(1-methylethyl)-2-(2-methyl-1-oxopropoxy)-γ-phenyl-, iodide, (γR)- (9CI) (CA INDEX NAME)

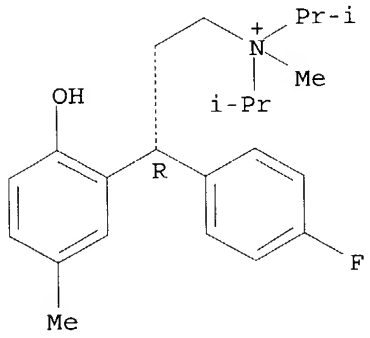
Absolute stereochemistry.



● I^-

RN 518360-91-3 HCAPLUS
CN Benzenepropanaminium, γ-(4-fluorophenyl)-2-hydroxy-N,5-dimethyl-N,N-bis(1-methylethyl)-, bromide, (γR)- (9CI) (CA INDEX NAME)

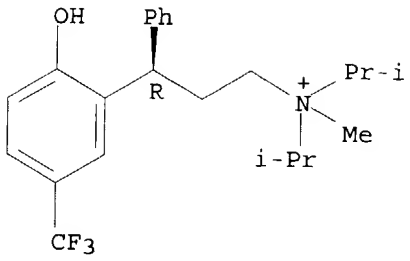
Absolute stereochemistry.



● Br^-

RN 518360-92-4 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-N-methyl-N,N-bis(1-methylethyl)-γ-phenyl-5-(trifluoromethyl)-, bromide, (γR)- (9CI) (CA INDEX NAME)

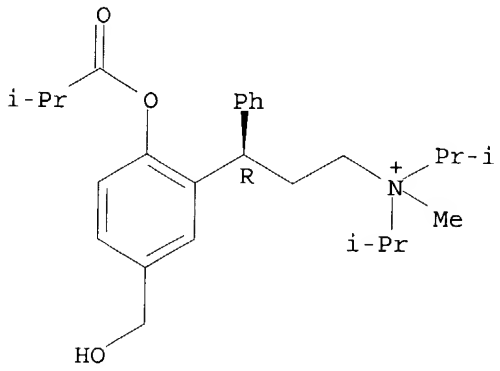
Absolute stereochemistry.



● Br^-

RN 518360-93-5 HCAPLUS
CN Benzenepropanaminium, 5-(hydroxymethyl)-N-methyl-N,N-bis(1-methylethyl)-2-(2-methyl-1-oxopropoxy)-γ-phenyl-, bromide, (γR)- (9CI) (CA INDEX NAME)

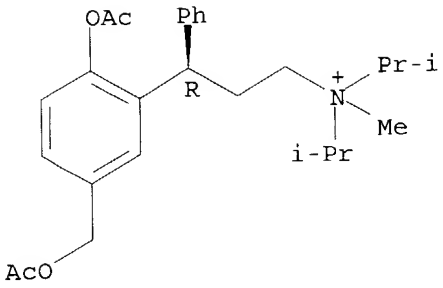
Absolute stereochemistry.



● Br^-

RN 518360-94-6 HCAPLUS
CN Benzenepropanaminium, 2-(acetyloxy)-5-[(acetyloxy)methyl]-N-methyl-N,N-bis(1-methylethyl)-γ-phenyl-, bromide, (γR)- (9CI) (CA INDEX NAME)

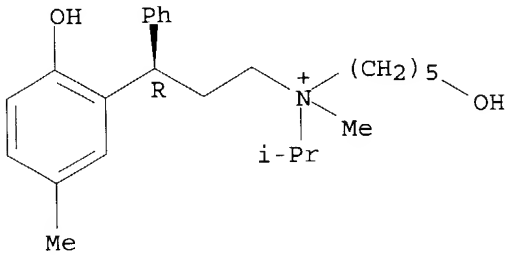
Absolute stereochemistry.



● Br^-

RN 518360-95-7 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-N-(5-hydroxypentyl)-N,5-dimethyl-N-(1-methylethyl)-γ-phenyl-, iodide, (γR)- (9CI) (CA INDEX NAME)

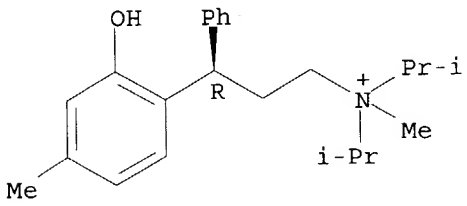
Absolute stereochemistry.



● I^-

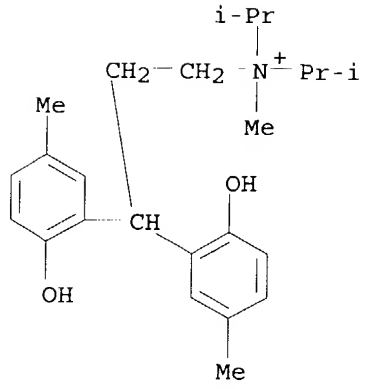
RN 518360-96-8 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-N,4-dimethyl-N,N-bis(1-methylethyl)-γ-phenyl-, iodide, (γR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● I^-

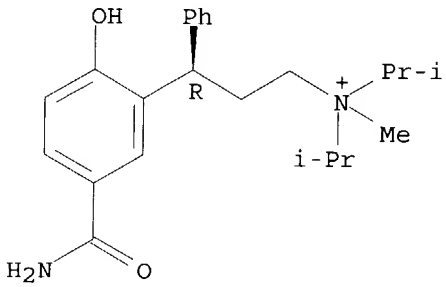
RN 518360-97-9 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-γ-(2-hydroxy-5-methylphenyl)-N,5-dimethyl-N,N-bis(1-methylethyl)-, iodide (9CI) (CA INDEX NAME)



● I⁻

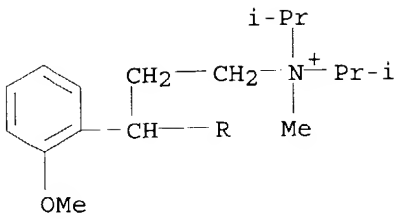
RN 518360-98-0 HCAPLUS
CN Benzenepropanaminium, 5-(aminocarbonyl)-2-hydroxy-N-methyl-N,N-bis(1-methylethyl)-γ-phenyl-, iodide, (γR)- (9CI) (CA INDEX NAME)

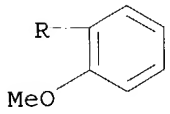
Absolute stereochemistry.



● I⁻

RN 518360-99-1 HCAPLUS
CN Benzenepropanaminium, 2-methoxy-γ-(2-methoxyphenyl)-N-methyl-N,N-bis(1-methylethyl)-, iodide (9CI) (CA INDEX NAME)

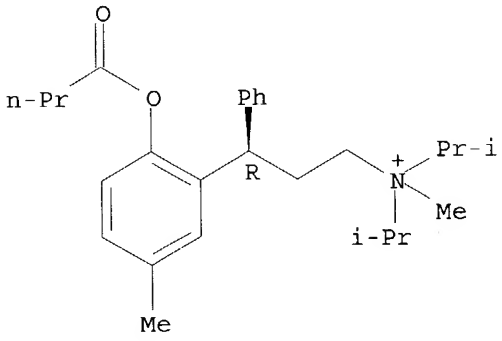




● I^-

RN 518361-00-7 HCAPLUS
CN Benzenepropanaminium, N,5-dimethyl-N,N-bis(1-methylethyl)-2-(1-oxobutoxy)-γ-phenyl-, iodide, (γR)- (9CI) (CA INDEX NAME)

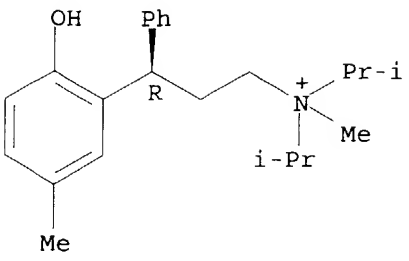
Absolute stereochemistry.



● I^-

RN 519038-88-1 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-N,5-dimethyl-N,N-bis(1-methylethyl)-γ-phenyl-, chloride, (γR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



● Cl^-

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:869590 HCAPLUS
DOCUMENT NUMBER: 137:363087
TITLE: Novel anticholinergic compounds for the treatment of incontinence and other disorders
INVENTOR(S): Druzgala, Pascal
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 21 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002169208	A1	20021114	US 2002-116202	20020403
CA 2443346	AA	20021205	CA 2002-2443346	20020403
WO 2002096855	A2	20021205	WO 2002-US10614	20020403
WO 2002096855	A3	20030213		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1383730	A2	20040128	EP 2002-774092	20020403
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004532874	T2	20041028	JP 2003-500035	20020403

PRIORITY APPLN. INFO.:
US 2001-281134P P 20010403
US 2002-350516P P 20020118
WO 2002-US10614 W 20020403

OTHER SOURCE(S): MARPAT 137:363087

AB In a preferred embodiment, the subject invention concerns novel analogs of oxybutynin. The present invention also concerns methods for synthesizing the oxybutynin analogs of the present invention. The invention also

pertains to methods for treating patients suffering from incontinence and other conditions.

IC ICM A61K031-225
ICS C07C069-76

NCL 514547000

CC 1-11 (Pharmacology)

IT 475090-48-3 475090-49-4 475090-50-7 475090-51-8 475090-52-9
475090-53-0 475090-54-1 475090-55-2 475090-56-3
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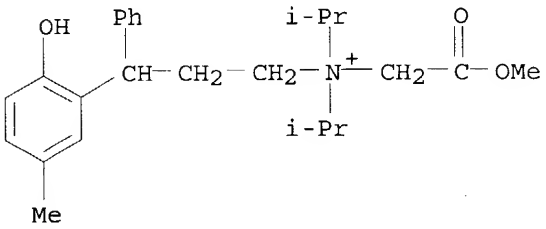
475091-12-4 475091-13-5 **475091-14-6** 475091-15-7
475091-16-8
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel anticholinergic compds. for treatment of incontinence and other disorders)

IT **475090-53-0 475091-14-6**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel anticholinergic compds. for treatment of incontinence and other disorders)

RN 475090-53-0 HCAPLUS
CN Benzenepropanaminium, 2-hydroxy-N-(2-methoxy-2-oxoethyl)-5-methyl-N,N-bis(1-methylethyl)-γ-phenyl- (9CI) (CA INDEX NAME)



RN 475091-14-6 HCAPLUS
CN Benzenepropanaminium, 5-[(acetyloxy)methyl]-2-hydroxy-N-(2-methoxy-2-oxoethyl)-N,N-bis(1-methylethyl)-γ-phenyl- (9CI) (CA INDEX NAME)